cells. Cytotoxicity of these compounds implies to use low non-toxic concentrations which render them less effective.

WO2013/1077559 describes modified monosaccharide compounds, such as the specific compound 8-azido-3,8-dideoxy-D-manno-octulosonic acid (also called herein "KDO-N_3) in methods for labeling specifically living microorganisms. The labeled living microorganisms have been limited to unicellular prokaryotic microorganisms (bacteria).

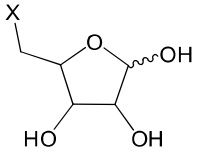
WO2016/177712 also describes modified monosaccharide compounds, such as the specific compound 5-azido-5-deoxy-D-arabinofuranose (also called herein "Ara-N_3) in methods for labeling specifically living microorganisms. The labeled living microorganisms have been limited to unicellular prokaryotic microorganisms (bacteria) and unicellular eukaryotic microorganisms (yeast, fungi and amoebas).

However, so far, no explanation can be provided on how and where said monosaccharide compounds are assimilated by cellular membranes of said microorganisms.

There is a constant need to find and develop new candidates, especially for labeling and detecting eukaryotic cell from multicellular organisms, to provide methods for identifying or isolating cancer cells, and to provide methods of diagnosis or cell therapy, particularly in the cancer field.

SUMMARY

The present disclosure is based on monosaccharides compounds of formula (I) or a precursor thereof:



(I),

in which X is a reactive group allowing to covalently link a further compound, such as a label or an anti-cancer drug or particles comprising an anti-cancer drug, via a click chemistry reaction. The formed conjugates may be thus implemented in methods for

labeling or detecting eukaryotic cells from a multicellular organism, for identifying or isolating cancer cells, or for treating a cancer.

More particularly, the inventors have found that assimilation of the monosaccharides compounds of formula (I), especially Ara-N_3, occurs with eukaryotic cell from a multicellular organism. They have also found that such assimilation in tumoral eukaryotic cells was different from non-tumoral eukaryotic cells and also more important compared to non-tumoral cells (in particular for bladder, blood, skin, pancreas, brain, liver, kidney, lung, muscle, lymphocyte, prostate, stomach, breast cancer compared to non-cancer cells). Therefore, the monosaccharides compounds of formula (I) and the precursors thereof can also be used as cancer probes and markers which can be useful for identifying, isolating or targeting cancer cells, and/or for diagnosing a cancer in a subject.

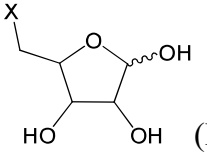
In one aspect, the present disclosure relates to an *in vitro* method for labeling or detecting or targeting an eukaryotic cell from a multicellular organism, the method comprising the steps of:

a) contacting a sample comprising eukaryotic cells with at least one modified monosaccharide compound or a precursor thereof;

b) contacting the sample of step (a) with a compound bearing a first reactive group, optionally in presence of copper; and

c) optionally detecting the compound of step (b) bond to the monosaccharide of step (a), as to detect eukaryotic cells;

wherein said at least one modified monosaccharide compound has the following formula (I):



(I),

in which X is a second reactive group, the first and the second reactive groups being able to react together in a click chemistry reaction.

In another aspect, the present disclosure relates to an *in vitro* or *ex vivo* method for identifying or isolating cancer cells, wherein said method comprises implementing a

method as described herein. In yet another aspect, the present disclosure relates to an *in vitro* or *ex vivo* method for diagnosing a cancer in a subject, wherein said method comprises implementing a method as described herein.

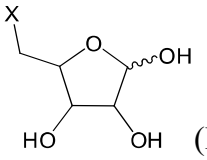
Accordingly, an example of the present disclosure is a method, preferably an *in vitro* method, for labeling or detecting or targeting an eukaryotic cell from a multicellular organism, the method comprising the steps of:

a) contacting a sample comprising eukaryotic cells with at least one modified monosaccharide compound or a precursor thereof;

b) contacting the sample of step (a) with a compound bearing a first reactive group, optionally in presence of copper; and

c) optionally detecting the compound of step (b) bond to the monosaccharide of step (a), as to detect eukaryotic cells;

wherein said at least one modified monosaccharide compound has the following formula (I):



(I),

in which X is a second reactive group, the first and the second reactive groups are able to react together in a click chemistry reaction, as to obtain the compound of step (b) bond to the said monosaccharide. In a preferred embodiment, the first reactive group is an alkyne group and the second reactive group X is an azido group ($-N_3$).

A further aspect of the disclosure is a kit for implementing the method for labeling, detecting or targeting an eukaryotic cell as defined herein, comprising:

- a modified monosaccharide compound of formula (I) or a precursor thereof, preferably of formula (I'), and
- a compound bearing a first reactive group.

A further example of the disclosure is a method for identifying or isolating cancer cells or for diagnosing a cancer in a subject, comprising implementing a method for labeling,

detecting, or targeting an eukaryotic cell from a multicellular organism, as defined herein, from said subject, preferably in a biological sample from said subject.

In another aspect, the present disclosure relates to a pharmaceutical composition comprising an eukaryotic cell presenting on its surface at least one modified monosaccharide compound of formula (I) or a precursor thereof, preferably of formula (I'), as defined herein, optionally linked operably or not to an anti-cancer drug or to particles comprising an anti-cancer drug.

A further example of the disclosure is a composition comprising an eukaryotic cell presenting on its surface at least one modified monosaccharide compound of formula (I) or a precursor thereof, preferably of formula (I'), as defined herein, operably linked or not to an anti-cancer drug or to particles comprising at least one anti-cancer drug. Another example is a pharmaceutical composition comprising such cell. Another example is such pharmaceutical composition for use in treating a cancer, especially by cell-based therapy. Another example is such pharmaceutical composition for use in diagnosing a cancer.

In yet another aspect, the disclosure relates to the pharmaceutical composition as defined herein, for use in therapy. In yet another aspect, the disclosure relates to use of the pharmaceutical composition as defined herein in the manufacture of a medicament for treating or diagnosing a cancer.

Another example of the disclosure is a method for treating a cancer in a subject in need thereof, comprising administering to said subject an efficient amount of a composition, as defined herein, comprising an eukaryotic cell presenting on its surface at least one modified monosaccharide compound of formula (I) or a precursor thereof, preferably of formula (I'), as defined herein, operably linked to an anti-cancer drug or to particles comprising at least one anti-cancer drug.

In another aspect, the disclosure relates to use of a modified monosaccharide compound or a precursor thereof as defined herein for medical imaging or diagnosis, preferably for medical imaging or diagnosing a cancer. A further example of the disclosure is a use of a

modified monosaccharide compound or a precursor thereof as defined herein for medical imaging or diagnosis, preferably for diagnosing a cancer, optionally with a compound bearing a first reactive group.

CLAIMS

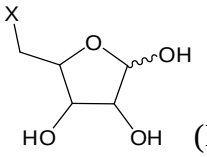
1. An *in vitro* method for labeling or detecting or targeting an eukaryotic cell from a multicellular organism, the method comprising the steps of:

a) contacting a sample comprising eukaryotic cells with at least one modified monosaccharide compound or a precursor thereof;

b) contacting the sample of step (a) with a compound bearing a first reactive group, optionally in presence of copper; and

c) optionally detecting the compound of step (b) bond to the monosaccharide of step (a), as to detect eukaryotic cells;

wherein said at least one modified monosaccharide compound has the following formula (I):

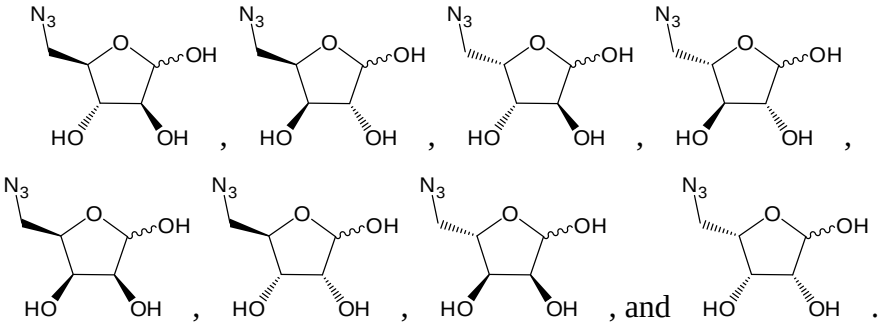


(I),

in which X is a second reactive group, the first and the second reactive groups being able to react together in a click chemistry reaction.

2. The method according to claim 1, wherein the second reactive group X is an azido group ($-N_3$) and the first reactive group is an alkyne group.

3. The method according to claim 1 or 2, wherein said at least one modified monosaccharide compound of formula (I) is selected in the group consisting of the following formulae:



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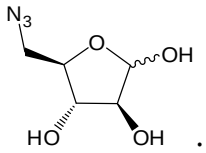
4. The method according to any one of claims 1 to 3, wherein said at least one modified monosaccharide compound of formula (I) is 5-azido-5-deoxy-D-arabinofuranose having the following formula:



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5. An *in vitro* or *ex vivo* method for identifying or isolating cancer cells, wherein said method comprises implementing a method according to any one of claims 1-4.

6. An *in vitro* or *ex vivo* method for diagnosing a cancer in a subject, wherein said method comprises implementing a method according to any one of claims 1-4.

7. The method according to claim 5 or 6, wherein the method further comprises the step of detecting the labeling, and optionally comparing the labeling to a reference level; and then identifying cancer cells or diagnosing a cancer based on the measuring of the label.

8. The method according to any one of claims 5 to 7, wherein the sample of step (a) is a biological sample from a subject, said subject having or being suspected to have cancer.

9. A kit for implementing the method for labeling or detecting or targeting an eukaryotic cell of anyone of claims 1 to 7 comprising:

- a modified monosaccharide compound of formula (I) or a precursor thereof, preferably of formula (I'), and
- a compound bearing a first reactive group.

10. A pharmaceutical composition comprising an eukaryotic cell presenting on its surface at least one modified monosaccharide compound of formula (I) or a precursor thereof, preferably of formula (I'), as defined in any one of claims 1 to 7, optionally linked operably or not to an anti-cancer drug or to particles comprising an anti-cancer drug.

11. The composition according to claim 10, wherein the anti-cancer drug is an antitumoral drug, preferably selected from the group consisting of chemotherapeutics, anti-cancer antibodies, hormonal therapy, immunotherapy, and kinase inhibitors.

12. The composition according to claim 10 or 11, wherein the cell is an isolated non-cancer cell, and preferably MSC.

13. The pharmaceutical composition as defined in claim 12, for use in therapy.

14. Use of the pharmaceutical composition as defined in claim 12 in the manufacture of a medicament for treating or diagnosing a cancer.

15. The method for diagnosing a cancer according to claim 5 or the pharmaceutical composition according to claim 13 or the use according to claim 14, wherein the cancer is chosen among rectal cancer, colorectal cancer, stomach cancer, head and neck cancer, thyroid cancer, cervical cancer, uterine cancer, breast cancer, ovarian cancer, brain cancer, lung cancer, skin cancer, bladder cancer, blood cancer, renal cancer, liver cancer, prostate cancer, multiple myeloma, and endometrial cancer.

16. Use of a modified monosaccharide compound or a precursor thereof as defined in any one of claims 1 to 4 for medical imaging or diagnosis, preferably for medical imaging or diagnosing a cancer.